IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Linhart, *et al.*

Appl. No. 10/026,914
Filed: December 27, 2001

For: Allergy Vaccines Containing Hybrid Polypeptides

Art Unit: 1645
Examiner: Jana A. Hines
Atty. Docket: 966927.00006 (0273-0006)

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Professor Rudolf Valenta, am an associate professor at the Division of Immunopathology (Department of Pathophysiology, University of Vienna, Austria), and I do hereby declare and state that:

1. I studied medicine at the University of Vienna and graduated with an MD degree in 1987.

2. Since 1988 I have been working at the Department of Pathophysiology (formerly: Department of General and Experimental Pathology) at the University of Vienna, Austria.

3. I extended my scientific experience during trainings in molecular biological techniques in the labs of Markus Susani (Institute of Molecular Biology, Salzburg, Austria) and Michael Breitenbach (Department of Genetics and Microbiology, University of Vienna) in 1988.

4. In 1992, I was awarded the qualification of a University lecturer for general and experimental pathology and became Head of the Molecular Immunopathology group at the Division of Immunopathology.

5. After a training in cellular mouse immunology in the lab of Alec Sehon (Department of Immunology, University of Manitoba, Winnipeg, Canada) and a one year's specialist training in Internal medicine and design of clinical studies at the Department of Hematology and the Department of Clinical Pharmacology of the University of Vienna in the years 1994 and 1995, I was granted a specialist degree for Pathophysiology in 1996.

6. In 1997, I completed my specialist training in immunology and became associate professor for Pathophysiology.

7. I have been Head of the Division of Immunopathology since December 2001 and have since headed the special research program: Molecular and immunological strategies for prevention, diagnosis and treatment of Type I allergies.

8. I have contributed to more than 200 peer-reviewed scientific papers, reviews, and book Chapters.

9. My work on the characterization of allergens and their use for new concepts of allergy treatment was granted numerous scientific awards, among others: the Sandoz Austria Award for Biology in 1994; the International Award of the Pharmacia Allergy Research Foundation in 1996; the START Award of the Austrian Science Fund in 1998; and the Sarstedt Science Award in 2000.

10. I have read and understood the Examiner's basis for rejection of the claims of the above-captioned Application, in the June 15, 2006, Office Actions particularly the 35 U.S.C. § 103(a) rejection over Ball et al., (WO 95/34578) in view of Vrtala et al., (1996: J. Allerg Clin. Immun. Vol 97(3): 781-787).

11. I have read and understood the disclosure and teachings of the Ball et al. reference (Same as US 6,008,340) particularly in reference to fusion polypeptides of Phl p1 epitopes and one other additional polypeptide.

12. Essentially Ball et al. teaches the use of "fusion polypeptides of Phl p1 epitopes and one other polypeptide," wherein that other polypeptide is used to drive the expression process and purification process. (See US 6,008,340 Col. 3, lines 1-6; Col. 5, lines 59 -62; and Col. 8, lines 15-31).

13. Ball et al. failed to teach or suggest that the fusion polypeptide of Phl p1 epitopes and another polypeptide that can be expressed as a fusion protein in prokaryotic or eukaryotic cells can be used as an immunotherapeutic agent.

14. In fact, Ball et al. failed to teach or suggest the fusion polypeptide of Phl p1 epitopes with a second polypeptide, which is itself an allergen.

15. In fact, Ball et al. failed to teach or suggest the fusion polypeptide of Phl p1 epitopes to a second, third, fourth etch polypeptide, all of which are allergens.

16. In contrast, the present invention teaches that one or more recombinant produced timothy grass pollen allergens can be fused and said fusion protein can be used as immunotherapeutic agent and moreover that the immunogenicity of each of the components of the fusion protein are increased through the fusion described in the present invention.

17. In fact, the inventors are surprised that fusion proteins of naturally occurring allergens can be used as immunotherapeutic agents and exhibit increased immunogenicity.

18. This surprising result is the subject of much speculation as to whether the fusion of allergens in some way destroys certain epitopes in the fusion allergen compared to the native unfused allergens.

19. To validate this surprising discovery, we tested whether immunization with the fusion allergens induces IgG antibodies (IgE-blocking antibodies) that recognize the individual allergen components.

20. As demonstrated in Figure 5 of the instant specification, the average IgG1 responses induced by the hybrid molecules to each of the individual allergens (rPhl p1, rPhl p2, rPhl p5, rPhl p6) were higher than those obtained by immunization with the single allergen components.

21. To further validate this surprising discovery, we tested whether mouse antibodies induced with the hybrid molecules can block the binding of grass pollen allergic patient's IgE antibodies to purified grass pollen allergens.

22. As shown in Tables 3A and 3B of the instant specification, IgG antibodies induced with the rP2-P6 and the rP6-P2 fusion proteins caused a 48%-54% inhibition of IgE binding to Phl p2 and a 54% to 67% inhibition of IgE binding to Phl p6 (Table 3A). By contrast, the inhibition of IgE reactivity yielded by preincubation with antibodies induced with rPhl p2 and rPhl p6 alone was very low (0-15%). (Table 3A).

All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patents ensuing thereon.

Respectfully submitted,

Date: 27. JULI, 2006

Professor Rudolf Valenta
Vienna General Hospital
Center of Physiology and Pathophysiology
Department of Pathophysiology
Division of Immunopathology
AKH-EBO 3Q
Währinger Gürtel 18-20
1090 Vienna, Austria